Hepatitis C Position Statement: Taking a Stand and Standing by it

Sir,

We refer to the comments of Aljudaibi[1] in relation to the Saudi Association for the Study of Liver Diseases and Transplantation (SASLT) Position Statement on the treatment of chronic hepatitis C virus (HCV).[2] Although we greatly value the author's comments, certain aspects must be clarified and discussed in this context. First, our Position Statement is obviously what it aims to be, a position that we, the SASLT governing board and the authors, have taken. It is a position that we have endorsed in the setting of differing opinions and aims to be a guidepost to let regional practitioners know where we stand on a topic of recurring debate, where the options of managing HCV-related disease remain vast and, as a consequence, on some occasions, confusing. It must be understood that the SASLT Statement is our stand on an arguable viewpoint, where Aljudaibi is equally justified to have his own. Moreover, we certainly make no pretense in calling our Position a guideline document, which in turn is generally evidenced-based.

Second, on this backdrop, we refer to the author's contention against utilizing the 12-week regimen of sofosbuvir and simeprevir for treating HCV genotype (GT)-4 infected patients, plus ribavirin (RBV) in those with cirrhosis.[3] A similar argument is made for the combination of sofosbuvir and daclatasvir, with the addition of RBV in those who are treatment-experienced cirrhotics.[3] However, our Position is no different than international guideline recommendations where these regimens feature prominently,[3,4] despite a lack of clinical evidence in GT4. This approach is based on extrapolating data from GT1 trials, given the observed antiviral effectiveness of sofosbuvir, simeprevir, and daclatasvir against GT4. Furthermore, RBV may be added in difficult-to-treat patients (such as treatment-experienced cirrhotics),[3] a distinction we make clearly in our Position.

On the other hand, Aljudaibi suggests adopting the regimen combining sofosbuvir and RBV, which although is evidence-based, but is also more expensive, and requires a longer duration of therapy (24 weeks). Hence, in our opinion, it is not an ideal choice. Certainly, there are many HCV treatment regimens that could be justifiably adopted; however, the basic premise of our Statement was to advance only a few that, in the authors' opinion are more valid, and may be applicable for the vast majority of patients with advanced fibrosis and cirrhosis (F3, F4) in a population overwhelmingly harboring GT1/4.

Third, Aljudaibi takes exception to the view that not all regimens in our Position are equally efficacious. This may be true to an extent since different genotypes exhibit different rates of sustained virologic response (SVR), and in a mixed bag of apples and oranges, it would be inappropriate to make comparisons, particularly in the absence of head-to-head studies. Nonetheless, we have distinctly stated that individualization of treatment regimens must be undertaken to maximize treatment benefit whereby a regimen, for instance, that is more appropriate for GT1 may not be applicable for GT3.

Fourth, the author points out that paritaprevir, ritonavir, ombitasvir, and RBV combination regimen has not yet been studied in HCV GT4 cirrhotics. While this is certainly true, this regimen has shown high SVR rates in GT4 (F0–F3) patients[5] and similar efficacy (with the addition of dasabuvir) in GT1 cirrhotic patients.[6] In an era of data extrapolation, we believe that this regimen would also be efficacious in GT4 cirrhotic patients, although it remains to be determined which of the treatment durations of 12, 16, or 24 weeks is appropriate.[7] Until these results become available, we prefer to err on the side of caution by extending therapy to 24 weeks. Similarly, we believe that null responder GT1 cirrhotics constitute a niche group with poor response characteristics. Despite evidence suggesting that the addition of RBV to the sofosbuvir/ledipasvir 12-week regimen can be used as an alternative option to 24 weeks of sofosbuvir/ledipasvir (without RBV) in treatment-experienced GT1 cirrhotic patients,[8] we believe that treatment extension to 24 weeks is preferable. Results in HCV GT1 cirrhotics treated for 12 or 24 weeks were not stratified for prior null response, and hence, the suitability of a 12-week regimen of sofosbuvir/ledipasvir with RBV in such patients remains unknown.

Finally, Aljudaibi points out that GT2/3 patients have not been adequately studied with many of these all-oral regimens. By implication, the adoption of these regimens in the Statement would be unjustified. While we openly acknowledge this, it remains that GT2/3 patients form a small minority of the HCV population pool in Saudi Arabia,[2] and we believe that (for matters of conciseness and readability) it would be redundant to cite separate recommendations for this small pool of patients. Moreover, some of the proposed options have been explored in GT3, albeit with lower SVR rates in patients with cirrhosis.

Faisal M. Sanai[1,2], Abdullah S. Alghamdi[3], Mohammed Y. Alghamdi[4]

[1]Department of Medicine, Division of Gastroenterology, King Abdulaziz Medical City, [3]Department of Medicine, Gastroenterology Unit, King Fahad Hospital, Jeddah, [2]Liver Disease Research Center, Riyadh, [4]Department of Gastroenterology, King Fahad Military Medical Complex, Dhahran, Saudi Arabia
E-mail: sanaifa@ngha.med.sa

REFERENCES

1. Al-Judaibi B. Ribavirin-free treatment may soon be a reality. Saudi J Gastroenterol 2015;21:260-1.
2. Alghamdi AS, Alqutub A, Abaalkhail F, Sanai FM, Alghamdi H, Altraif I, *et al*. SASLT position statement on the direct-acting antiviral agents for the treatment of hepatitis C virus infection. Saudi J Gastroenterol 2015;21:60-3.
3. European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C 2014. J Hepatol 2014;61:373-95.
4. AASLD/IDSA/IAS-USA. Recommendations for testing, managing, and treating hepatitis C. Available from: http://www.hcvguidelines.org. [Last accessed on 2015 Feb 13].
5. Hézode C, Asselah T, Reddy KR, Hassanein T, Berenguer M, Fleischer-Stepniewska K, *et al*. Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naive and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): A randomised, open-label trial. Lancet 2015;385:2502-9.
6. Poordad F, Hezode C, Trinh R, Kowdley KV, Zeuzem S, Agarwal K, *et al*. ABT-450/r-ombitasvir and dasabuvir with ribavirin for hepatitis C with cirrhosis. N Engl J Med 2014;370:1973-82.
7. A Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Ombitasvir/ABT-450/Ritonavir Co-administered With Ribavirin (RBV) in Adults with Genotype 4 Chronic Hepatitis C Virus (HCV) Infection and Cirrhosis. Available from: http://www.Clinicaltrials.gov. [Last accessed on 2015 Jun 4].
8. Bourlière M, Bronowicki JP, de Ledinghen V, Hézode C, Zoulim F, Mathurin P, *et al*. Ledipasvir-sofosbuvir with or without ribavirin to treat patients with HCV genotype 1 infection and cirrhosis non-responsive to previous protease-inhibitor therapy: A randomised, double-blind, phase 2 trial (SIRIUS). Lancet Infect Dis 2015;15:397-404.

Access this article online

Quick Response Code:

Website: www.saudijgastro.com

DOI: 10.4103/1319-3767.161637